
Contextual effect of repression of bone morphogenetic protein activity in prostate cancer.

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Public Summary:

The overall impact of BMP signaling on prostate tumors is likely to be an amalgam of its effect on the tumor cells, on the stromal cells in the tumor microenvironment, and on the heterotypic interactions that occur between the various cell types present in the tumor organ.

Scientific Abstract:

Several studies have focused on the effect of bone morphogenetic protein (BMP) on prostate cancer homing and growth at distant metastatic sites, but very little effect at the primary site. Here, we used two cell lines, one (E8) isolated from a primary tumor and the other (cE1) from a recurrent tumor arising at the primary site, both from the conditional Pten deletion mouse model of prostatic adenocarcinoma. Over-expression of the BMP antagonist noggin inhibited proliferation of cE1 cells in vitro while enhancing their ability to migrate. On the other hand, cE1/noggin grafts grown in vivo showed a greater mass and a higher proliferation index than the cE1/control grafts. For suppression of BMP activity in the context of cancer-associated fibroblasts (CAFs), we used noggin-transduced CAFs from the same mouse model to determine their effect on E8- or cE1-induced tumor growth. CAF/noggin led to increased tumor mass and greater de-differentiation of the E8 cell when compared with tumors formed in the presence of CAF/control cells. A trend of increase in the size of the tumor was also noted for cE1 cells when inoculated with CAF/noggin. Together, the results may point to a potential inhibitory role of BMP in the growth or re-growth of prostate tumor at the primary site. Additionally, results for cE1/noggin, and cE1 mixed with CAF/noggin, suggested that suppression of BMP activity in the cancer cells may have a stronger growth-enhancing effect on the tumor than its suppression in the fibroblastic compartment of the tumor microenvironment.

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